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Thermoregulatory Responses to Cold Transients: Effects of Two Clothing Systems in Resting Women

U S ARMY RESEARCH INSTITUTE OF ENVIRONMENTAL MEDICINE
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This report focuses on development of a thermoregulatory model useful for forecasting heat exchange properties, shivering thermogenesis, and body temperature response in women wearing protective clothing. Six female, nonsmokers (18-29 yr), resting supine, were exposed to a cold ramp ($T_a = \bar{T}_r = 20°C$ to $-5°C$, $-0.32°C/min$, $V=1 m \cdot s^{-1}$) in the follicular phase (F=days 2-6) and in the luteal phase (L= days 19-23) of their menstrual cycle. Subjects wore either Battle Dress Uniforms (BDU) or Battle Dress Overgarment over the BDU with thermal resistances of $R_T = 0.2$ and $0.4\ m^2 \cdot K \cdot W^{-1}$, respectively. Esophageal temperature (T_{es}) rose during the cold ramps. Shivering thermogenesis ($\Delta M = M - M_{basal}, W \cdot m^{-2}$) was correlated ($r^2 = 0.9$) with reduced mean weighted skin ($\bar{T}_{sk}$, six sites) and finger temperature ($T_{fing,}$ under a work glove). Menstrual cycle stage and clothing resistance were significant ($P \leq 0.05$) modifiers of the rate of heat debt based on partitional calorimetry determined from M, body weight, surface area, T_{es}, and $\bar{T}_{sk}$. Thermal information from extremities and variations in body heat content during a given menstrual phase, independent from core and $\bar{T}_{sk}$, must be considered in any thermoregulatory model quantifying ΔM effects in resting women exposed to cold stress. Several cold-air models which incorporate %Body Fat, core and skin temperature inputs were fairly reliable predictors of shivering response over a limited scope of operational and environmental levels.

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This report looks into the development of a thermoregulatory model useful in the cold. We used transient analysis for implementing the cold stress and ascertaining a given thermoregulatory response. Typically, in the transient approach a person is exposed to a gradual change in ambient stress rather than a step change (movement from one environment to a totally different one in rapid succession). Rather than shocking the thermal system to elicit a given efferent physiological modification, transient thermal analysis allows the step-by-step development and appearance of threshold values owing to efferent thermoregulatory reactions. During the resting state in the cold, the major response is related to shivering (by excess metabolic heat production) principally from a drop in skin and core temperatures. The challenge is to investigate discrete thresholds and magnitude based on a slope analysis of the efferent thermal response. Quantification of key dependent variables that go into mathematical algorithm development, as a function of the body's homeostatic thermoregulatory drives can be determined. Using a repeated measures approach in which a series of individuals go through a series of equivalent ambient temperature ramps, many subtle, inherent variables which affect a response such as stages of the menstrual cycle or effect of clothing thermal resistance on a person, during a given experiment, are factored into the transient analysis. Peripheral and internal temperature sensitivities can also be estimated by using a singular, replicable ambient temperature change while controlling other variables. A modeling technique such as maximum likelihood parameter estimation can be used to quantify those thermal factors eliciting a response above basal levels. The maximum likelihood parameter estimation algorithm can then be compared to other model approaches which predict shivering response to assorted variables. To our knowledge this is the first approach of its kind to employ the technique in ascertaining effect of stages of the menstrual cycle to a thermal challenge.

ACKNOWLEDGMENTS

The authors acknowledge the efforts of all the volunteers in this study. We also acknowledge the professional efforts of Ms. Nisha Charkoudian, Mrs. Janet E. Staab, Ms Jane P. Deluca, and Mr. Robert F. Wallace in supporting the collection, data reduction, graphical presentation, general biochemical, and statistical analyses of the data.

This study was funded, in part, by a Congressional Special Interest Medical Research Program focused on Defense Women's Health.

EXECUTIVE SUMMARY

This report focuses on development of a thermoregulatory model useful for forecasting heat exchange properties, shivering thermogenesis, and body temperature response in women wearing protective clothing. Six female, nonsmokers (18-29 yr), resting supine, were exposed to a cold ramp ($T_a = \bar{T}_r = 20°C$ to $-5°C$, $-0.32°C/min, V=1 m \cdot s^{-1}$) in the follicular phase (F=days 2-6) and in the luteal phase (L= days 19-23) of their menstrual cycle. All stages of the menstrual cycle were verified by *post hoc* blood analyses of estradiol and progesterone levels. The subjects were clothed in either Battle Dress Uniform (BDU) or Battle Dress Overgarment over the BDU with thermal resistances of $R_T = 0.2$ and $0.4\ m^2 \cdot K \cdot W^{-1}$, respectively. Extensive peripheral vasoconstriction occurred during the ramp, elevating resting esophageal temperature (T_{es}) by +0.2°C. Shivering thermogenesis ($\Delta M = M - M_{basal}, W \cdot m^{-2}$) modeled by maximum likelihood parameter estimation was tightly correlated ($r^2 = 0.9$) with reduced mean weighted skin ($\bar{T}_{sk}$, six sites) and finger temperature (T_{fing}, under a work glove). T_{fing} was a significant peripheral multiplier of the response. T_{fing} and $\bar{T}_{sk}$ thresholds in F (26.5°C & 32.5°C, respectively), modifying ΔM, were offset by -5°C and -1.5°C in L phase ($P \leq 0.002$) when wearing the BDU. Cold-induced vasodilation (CIVD) observed in T_{fing} (3 of 6 women) lagged in time during the luteal phase. Menstrual cycle stage and clothing resistance (R_T) were significant ($P \leq 0.05$) modifiers of the rate of heat debt based on partitional calorimetry determined from M, body weight, surface area, T_{es}, and $\bar{T}_{sk}$. Our data show that thermal information from extremities and variations in body heat content during a given menstrual phase, independent from core and $\bar{T}_{sk}$, must be considered in any thermoregulatory model quantifying ΔM effects in resting women exposed to cold stress. When it is not possible to integrate all these variables, several cold-air models which incorporate %Body Fat, core and skin temperature inputs can serve as fairly reliable predictors of shivering response over a limited scope of operational and environmental levels for either men or women.

INTRODUCTION

Background

The reproductive system has a clear and important role in modulating thermoregulation in women particularly when internal body temperature becomes elevated during the luteal phase compared to the follicular phase of the menstrual cycle. In the luteal phase, thermoregulatory responses of women (bounded within a tight reproductive age) are characterized by alterations in core temperature thresholds affecting the onset of specific physiological effector responses during exercise, heat exposure and cold exposure (Gonzalez and Nishi, 1976; Haslag and Hertzman, 1965; Hessemer and Brŭck 1985b; Kolka *et al.*, 1989; Stephenson and Kolka, 1985; Stephenson *et al.*, 1988; Stephenson *et al.*, 1989). Elevated core temperature thresholds controlling the onset of sweating and skin blood responses are consistent with a higher internal body temperature reference point evident in the luteal phase which may compromise thermoregulation during prolonged exercise or extreme heat exposure in the luteal phase (Pivarnik *et al.*, 1992; Stephenson and Kolka, 1988).

Little data exist quantifying female responses to cold stress. During cold stress, shivering by gross muscular contraction may or may not be sufficient to maintain core temperature. Core temperature and skin temperatures interact in a unique fashion either as constant temperature multipliers or in a summative fashion to increase metabolism. However, to date other than limited studies (Hessemer and Brŭck 1985a; Graham et al., 1989) there is a scarcity of quantitative research depicting cold responses in females. This lack is especially evident characterizing whether females in specific stages of the menstrual cycle display a differential "gain" in the shivering response in a plot of excess shivering (ΔM) against either integrated mean body temperature or core temperature (esophageal or rectal). Less exact is knowledge about the effects of prostaglandins and/or CNS responses to cytokines such as IL1-α and β or IL-6 that often modulate

thermoregulatory responses during a woman's luteal phase (Cannon and Dinarello, 1985;Scott et al.,1987). These cytokines might alter specific body temperature thresholds conceivably by altering the cellular dynamics inherent in warm, cold, or temperature insensitive neurons resident in the anterior hypothalamus, particularly during cold and heat stress.

Current research (Boulant, 1981;Boulant and Silva, 1989) shows that all afferent thermal signals, following a short time lag, are sensed and integrated by the preoptic/anterior hypothalamus. Hypothalamic neurons activating cold responses such as cutaneous vasoconstriction, shivering, and other forms of heat conservation (often behaviorally driven) become stimulated as well (Simon et al., 1986). Skin temperature is set by the extent of blood flow to a site, thermal conductivity, and environmental temperature and will reach a level imposed by the ambient conditions (Gonzalez *et al.*, 1978). When core temperature is offset to a higher temperature level in the luteal phase, there is often competitive inhibition in the processing of information between warm sensitive and cold sensitive neurons (Boulant and Gonzalez, 1977; Boulant, personal communication, 1996). This competition of thermal afferent information from central and peripheral receptors may or may not wholly blunt the shivering response to cold stress at a given mean skin temperature. During steady-state, there may be interaction of several factors inducing the response and the mechanisms frequently remain invisible. Thermal transients (using dynamic ambient temperature changes) are reliable ways of revealing mechanisms within a given physiological system (Gonzalez et al., 1981).

Generally, in order to maintain appropriate heat balance when core and skin temperatures are elevated, heat loss mechanisms become activated and there occurs increased sweat secretion and increased blood flow to the skin surface. But in the luteal phase of some eumenorrheic women, particularly during exercise, effect of transient cold stress integrated in the hypothalamus works counter to the latter response. Women may find themselves attempting to eliminate heat by evaporative heat loss or by sensible heat loss at some higher internal reference temperature (than their normal set point) in the face of skin thermoreceptors increasing afferent signals to the hypothalamus calling for initiation of shivering and enhanced heat conservation.

Burse (1979) pointed out that morphological differences of women (20% smaller body mass, 14% more body fat, 33% less lean body mass, but only 14-22% less surface area) impinge greatly on their relative ability to balance body heat production and losses. Initially, women have greater body insulation effective against cold temperature transients when fully vasoconstricted except on hands and feet which are susceptible to adrenergic and local mediating hormonal factors. The greater peripheral body 'shell' available as a heat sink to dump metabolic heat in average sized women, often occurs at the cost of a greater burden of body fat for heat to be transported (Buskirk et al., 1963; Nunneley, 1978). Despite a comparable percentage of body fat, lean body mass, and other anthropomorphic features, women may be more sensitive than men to the drops in ambient air temperatures.

The present experiments were designed to perturb the thermoregulatory system by a repeatable cold stress (Gonzalez et al., 1971;Gonzalez et al., 1981). The technique allows quantification of dynamic responses and provides information characterizing cold reactions in women when dressed in two separate military clothing systems with different thermal resistances. This report represents the results of an initial Defense Women's Health Research effort focusing on cold stress in the resting state and modeling aspects of the mechanisms revealed during thermal transients. This report addresses three major objectives:

A) Effective heat exchange responses in women clothed in two different clothing systems;

B) Magnitude of shivering thermogenesis as a function of thermoregulatory control during cold transients activated principally by changes in core and skin temperature during two stages of the menstrual cycle, and

C) Ways of modeling physiological characteristics embracing clothing properties.

METHODS AND PROCEDURES

Six, highly motivated volunteers, recruited from the military test subject pool, completed all experiments. Physical characteristics are shown in Table 1.

Table 1. **Physical Characteristics of the Female Volunteers.**

Subject	*Age (yr)*	*Height (m)*	*Weight (kg)*	*Body Surface Area (m^2)*	*%BF*	*LBM (kg)*
S1	21	1.73	70.5	1.83	25.1	52.8
S2	19	1.70	62.3	1.72	23.3	47.8
S3	19	1.66	56.0	1.61	21.6	43.9
S5	19	1.57	49.1	1.47	22.0	38.3
S6	20	1.68	59.5	1.67	23.1	45.8
S7	29	1.56	68.0	1.68	28.3	48.8
Mean	**21.2**	**1.65**	**60.9**	**1.66**	**23.9**	**46.2**
±SD	**3.9**	**0.1**	**7.9**	**0.12**	**2.5**	**4.9**

Experiments on each volunteer subject were done in the late fall, winter, and early spring. Each of the six female volunteers displayed a normal menstrual cycle as defined by regular periodicity and were not taking oral contraceptives. To verify ovulatory

menstrual cycles, each subject initially recorded her daily basal body temperature (BBT) upon awakening for a month and continued during the experimental periods. Oral temperature was measured twice at the same time each morning (mouth completely shut) using a calibrated, fast responding, automated oral thermometer. Data from an entire menstrual cycle were collected and graphed prior to the study to determine whether BBT increased after ovulation (Kleitman and Ramsaroop, 1948). Although BBT is not a wholly sufficient method to predict ovulation time, higher BBT is closely correlated with the higher plasma progesterone concentration evident in the luteal phase of the menstrual cycle (Cargille et al. 1969) and directly applicable to our resting study.

Testing in the luteal phase occurred only on days when the resting core temperature was elevated (approximate days 19-23). Testing in the early follicular phase occurred on days 2-6 (day 1 = first day of menstrual flow). All stages of the menstrual cycle were verified by *post hoc* blood analyses of estradiol and progesterone levels (Table 2).

Table 2. Mean (±1SD) concentration levels of estradiol and progesterone in the women subjects during rest.

	Estradiol $pg \bullet ml^{-1}$	**Progesterone** $ng \bullet ml^{-1}$
Follicular Phase day 2-6,n=6	30.2±12.9*	0.45±0.24*
Luteal Phase days 19-23, n=6	122.5±41.1*	9.90±4.64*

***(P≤0.0001 comparing Estradiol and Progesterone level between phases).**

Prior to the three days of testing, volunteers were thoroughly familiarized with all experimental techniques and had their standing height measured. During these training sessions body weights were measured so that on the four test days (twice in BDUs and

twice in BDOs), pre-experiment body weights could be easily traced back within 1% of the mean body weight measured during preliminary testing to control for possible effects of hypo-hydration. Before testing began, each subject had a pregnancy test completed and a negative report.

Experimental Testing:

Upon arriving at the laboratory each morning, a 10-ml blood sample was taken by venipuncture for the measurement of each subject's progesterone and estradiol concentrations (RIA) to accurately define menstrual cycle phases of each woman (see Table 2). After a blood draw, the previously instructed volunteer inserted a polyethylene-encased thermocouple through the nostril channeled through the pharynx into the esophagus to a depth about 1/4 of her height (in centimeters). Exact placement of the thermocouple at the mid-heart level was verified by following a real-time thermal recording on a computer screen as she slightly inserted and retracted the thermocouple into the esophagus past the initial "hot" spot demarcating a correct heart level point (Stephenson and Kolka, 1985).

Surface thermistors with calibrated heat flow disks were placed at six skin sites and area weighted to estimate mean skin temperature ($\bar{T}_{sk}$ Nishi and Gagge, 1970) as:

$$\bar{T}_{sk} = 0.35 \cdot T1 + 0.19 \cdot T2 + 0.20 \cdot T3 + 0.12 \cdot T4 + 0.07 \cdot T5 + 0.05 \cdot T6 \quad ,°C$$

where, T1= chest skin temperature

T2= thigh T3= calf T4= hand T5=upper arm

T6= mid-forearm

Separate fine gauge copper-constantan thermocouples were also placed in the middle finger nail bed and big toe nail bed. A calibrated heat flow transducer surrounding each embedded thermistor element determined heat flux from each of the skin sites. Weighted

heat flux ($W \cdot m^{-2}$) was calculated from each respective skin site area weighting (Chang et al., 1990;Ducharme et al.,1990).

Environmental temperatures, core and skin temperatures, and heat flow data were recorded every 15 seconds using a personal computer. Wind speed in the chamber was controlled at 1 $m \cdot s^{-1}$.

Oxygen uptake ($\dot{V}O_2$, $L \cdot min^{-1}$) was measured by collection of all expired gases into a 2-min Douglas bag, sampled every 20th min of the transient and twice at 20 °C, once prior to the decrease of ambient temperature and once after some 10-15 minutes period at -10 °C. Heat production ($W \cdot m^{-2}$) was calculated from the expired respiratory parameters obtained, the calorific equivalent of one liter of oxygen, and the DuBois surface area equation (Endrusick et al., 1992). Subjects were exposed to the lowest air temperature level (-10 °C) for some additional 10-15 minutes or until each was withdrawn because fingertip skin temperature reached ≤5 °C or if esophageal temperature reached ≤ 35 °C. These lower limits were advisory guidelines set by the HURC for removal of a given subject from the test for that day.

Heart rates were obtained and recorded every five minutes from the electrocardiogram measured continuously using chest electrodes (CM 5 placement) interfaced to a telemetry system (Hewlett-Packard 78510A&B).

Subjects were asked to refrain from food, caffeine, and medication consumption ≈10h prior to the experimental testing. Body weight and composition were determined by repeated nude weighings and skin fold measurements (Endrusick et al., 1992).

Steady- State and Transient Exposure

All subjects rested on a specially designed wooden cot for 15 minutes of baseline data at 20°C air temperature. After complete instrumentation, a rest period began, lasting ~20-30 mins until equilibration occurred by having skin and core temperature remain constant within ± 0.1 °C for 10-15min. After the initial period, each subject was exposed to the thermal transient by having the environmental chamber ambient temperature ($T_a = \bar{T}$ = operative temperature, Gagge and Gonzalez, 1995) decrease in a repeatable downward ramp (Figure 1). Dew point temperature was allowed to fall passively during the transient room temperature decline. This transient phase typically continued for 80-120 minutes (the latter time points when dressed in BDO+BDUs) at a constant decreased exponential ramping rate of -0.32 $°C \bullet min^{-1}$. A final exposure time of 10-20 mins at T_a of -5 to -10°C was completed before ending the experiments by a subject's request or in conformity with Human Use Review Committee (HURC) recommendations.

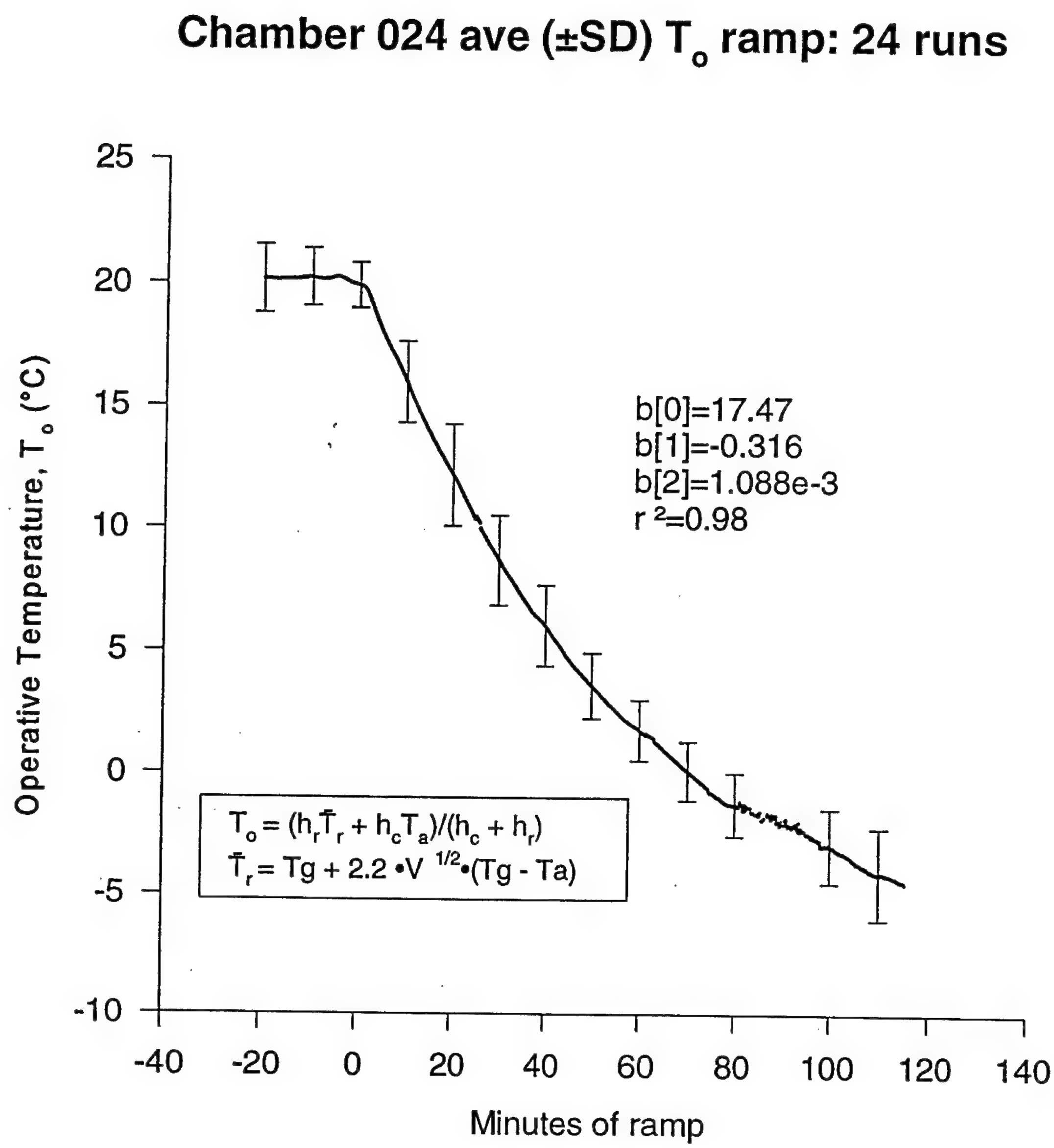


Figure 1. Determination of Operative (T_o) temperature during thermal transient experiments.

Rate of heat storage and integrated mean body temperature

In the cold, initial mean body temperature, $\bar{T}'_b$, is often calculated from a steady-state weighting ratio of mean skin temperature to rectal temperature $\{\bar{T}_{sk} : T_{re}\}$ as 1:2 . In the heat or during exercise, the probable ratio varies from 1:4 to 1:9 when esophageal or rectal temperature is used as measure of core temperature. During exercise or ambient temperature transients when body temperatures are in a non-steady state, coefficients for mean body temperature change appreciably (Livingstone, 1967; Gagge and Gonzalez, 1995). The calculation of the classical Burton (1935) mean body temperature by a simple weighting of core and skin temperature is inaccurate during thermal transients and probably not applicable in women since both time and ambient temperature as well as skin and core temperatures vary.

Rate of storage of body heat (S), evaluated by partitional calorimetry (Gagge and Gonzalez, 1995; Vallerand,et al., 1992; Bittel, 1987), is directly associated with the rate of change of integrated (i.e., weights both peripheral and central thermoreception) mean body temperature ($\Delta\bar{T}b/ \Delta t$). This form has been used to quantify responses particularly during cold stress (Vallerand, et al., 1992; Bittel and Henane, 1975; Gagge and Gonzalez, 1995), in which

$$S = (0.965 \bullet m_b / A_D) \bullet \Delta\bar{T}_b / \Delta t \qquad W \bullet m^{-2}$$

where 0.965 is the specific heat of the body in $W \bullet h \bullet {}^\circ C^{-1} \bullet kg^{-1}$ (or 3.49 $kJ \bullet {}^\circ C^{-1}\ kg^{-1}$) and m_b is the body weight in kg; Δt is time in hours.

For this study, during the resting period at T_a = 20 °C, prior to ambient temperature drops, initial mean body temperature, $\bar{T}'_{b,o}$, was first calculated by a 1:4 weighted average

of $\bar{T}_{sk}$ and esophageal (T_{es}) temperature. Integrated mean body temperature was then determined as

$$\bar{T}_b,i = \bar{T}'_{b,o} + \sum_0^t (\Delta\bar{T}_b / \Delta t)\, dt \quad °C$$

or $$= \bar{T}'_{b,o} + [(S \bullet A_D)/ (0.965 \bullet m_b)] \bullet \Delta t$$

where Δt is the interval time ($t_x - t_o$) of a run taken at each $\bar{T}_b$ (min/60) in hours. The ΔM and other dependent variables (heat flow, skin temperatures, and T_{es}) were compared to the $\bar{T}_b$,i by linear regression methods (SYSTAT, 1992). Appendix A gives a further explanation of the analysis used in this report.

Partitional calorimetric analyses (Gagge and Gonzalez, 1995; Vallerand et al., 1992) were conducted during each 20-minutes of an experiment taking into account each avenue of heat exchange from the heat balance equation (metabolic and respiratory and convective heat loss responses and of all respective clothing heat transfer coefficients) in which:

$$S = M - E_{sk} - (R \pm C) - K, \qquad [W \bullet m^{-2}]$$

where: S = rate of body heat storage described above; M = internal heat production, or metabolism from each 20min $\dot{V}O_2$ interval; E_{sk} = evaporation or insensible (wet) heat exchange which is set by the clothing moisture properties (i_m/clo) and

evaporative heat transfer coefficients determined from parallel copper manikin evaluations of the garments, the skin to ambient temperature gradient ($\bar{T}_{sk}$ - $T_{o)}$, and by the change in body weight loss and respiratory heat loss; R = radiation; C = convection; K = conduction. R and C combine as sensible (dry) heat exchange which is determined by the environment, thermal conductance and insulative properties of the uniforms and respective heat transfer coefficients.

Statistics

All data (esophageal and skin temperatures, heat flow, and ΔM) were analyzed by analysis of variance techniques with repeated measures (SYSTAT for Windows ,1992). Whenever a significant F-ratio was found, Tukey's critical difference was employed for post hoc analysis ($P < 0.05$). Additionally, maximum likelihood parameter estimation of the respective control coefficients (Brownlee, 1965; SYSTAT, 1992) was used to establish the thermoregulatory control of ΔM as a integrated function of T_{es},$\bar{T}_{sk}$, and finger (T_{fing}) temperatures as critical parameters during the cold transient. Influence of heat content and heat flux during the thermal transient was analyzed by two way (clothing resistance x menstrual phase) and 3 way (time x thermal resistance x menstrual phase) analysis of variance for repeated measures (SAS for Windows, 1990).

Clothing systems

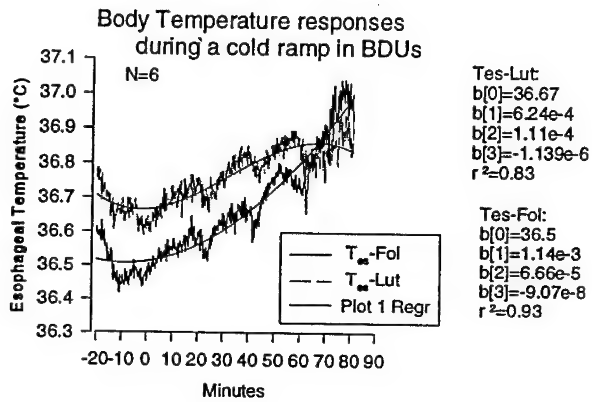
During the "BDU" experiments the women dressed in U.S. Army issue physical

training (PT) shorts and underwear plus the U.S. Army T-shirt worn underneath a Temperate Battle Dress Uniform (TBDU). The latter garments were worn underneath the U.S. Army Battle Dress Overgarment (BDU+BDO) during the set of experiments designated as "BDO-runs." The clothing insulation values were evaluated separately at three different wind speeds to establish effective clothing heat and mass transfer coefficients using a regional copper manikin resting supine on a wooden-framed cot supported by parachute nylon webbing which simulated conditions of the human experiments. The total thermal insulation value of the BDU system at 1 $m \cdot s^{-1}$ wind speed (paralleling the human experiments) was 1.33 clo (~0.21 $m^2 \cdot K \cdot W^{-1}$) and that of the BDO+BDU was 2.58 clo (~0.4 $m^2 \cdot K \cdot W^{-1}$). During all experiments, subjects also wore the standard US Army Light Duty Work Glove with a five-finger woolen insert, designated as "*LD*" with each configuration. The glove was separately evaluated on the USARIEM copper hand model and had a thermal insulation value of 0.86 clo (0.13 $m^2 \cdot K \cdot W^{-1}$). During all experiments, the standard issue US Army Black Boot and the US Army Cushion-Sole Sock were worn on the feet by the subjects with each clothing system. The thermal insulation of the boot with a sock was analyzed (1.8 clo; 0.28 $m^2 \cdot K \cdot W^{-1}$) using the USARIEM regional copper foot (Endrusick et al., 1992).

During all experiments, subjects were not allowed to open or ventilate their garments by opening closures, zippers, etc. or by excessive movement, thereby serving to control against disparate changes in body temperatures and heat flow.

RESULTS

Skin temperatures and Esophageal temperature responses. Extensive peripheral vasoconstriction and rate of fall in $\dot{T}_{sk}/\Delta t$ of some -0.1°C/min occurred during the decreasing temperature ramps, often elevating resting esophageal temperature (T_{es}) by 0.2 - 0.3 °C in the subjects when wearing the BDU (Figure 2).



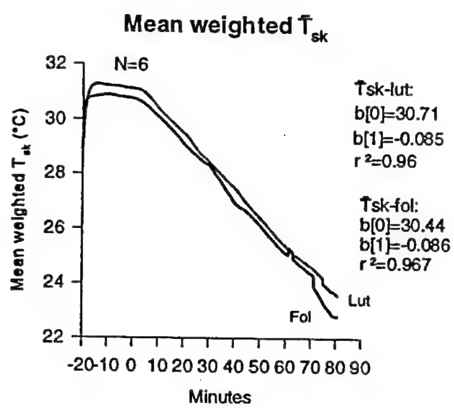


Figure 2. Esophageal (T_{es}) and mean weighted skin temperature ($\bar{T}_{sk}$) plotted as a function of minutes of cold ramp. Regression coefficients in the form $Y= b_o+ b_1X^1+b_2X^2 +..+b_nX^n$ with a coefficient of determination = r^2

Metabolic Heat Production

Shivering thermogensis described by ($\Delta M = M - M_{basal}$, $W \bullet m^{-2}$) was tightly correlated with the reduced mean weighted skin ($\bar{T}_{sk}$, six sites) and finger temperature (T_{fing}).

SS3-Follicular BDU (1.3 clo)

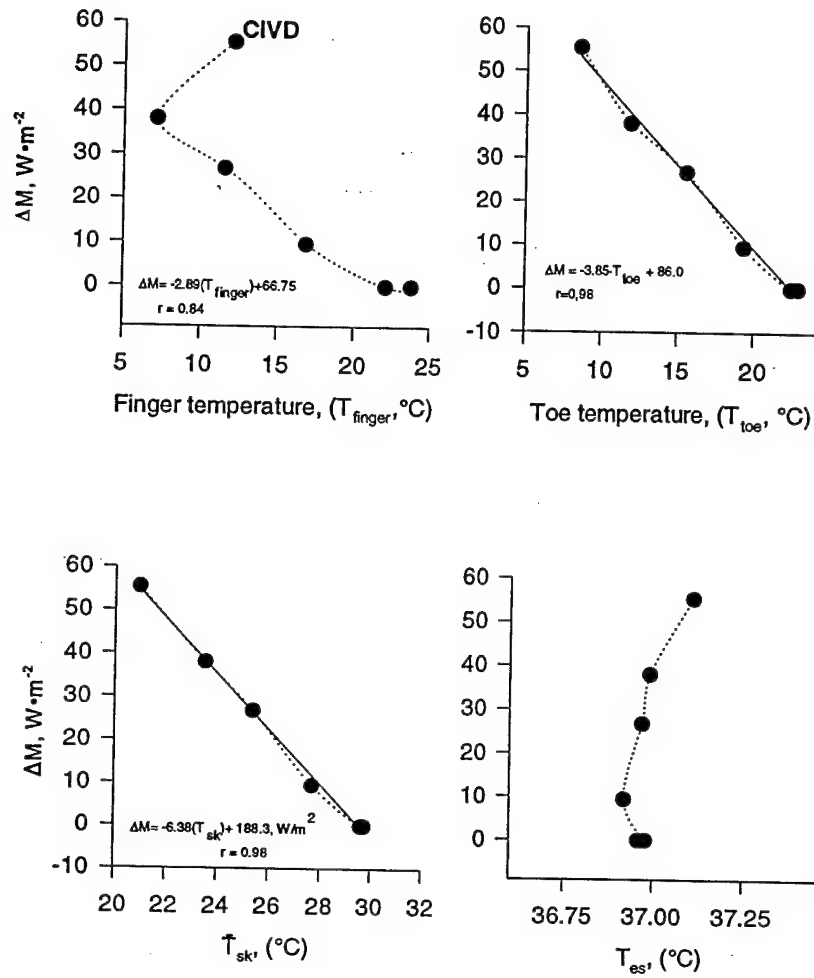


Figure 3. Shivering thermogenesis (ΔM) as a function of various body temperatures in a typical subject.

Figure 4 depicts the shivering thermogenesis (ΔM) plotted versus integrated mean body temperature from a typical subject studied in the follicular and luteal phases of her menstrual cycle while dressed in a BDU.

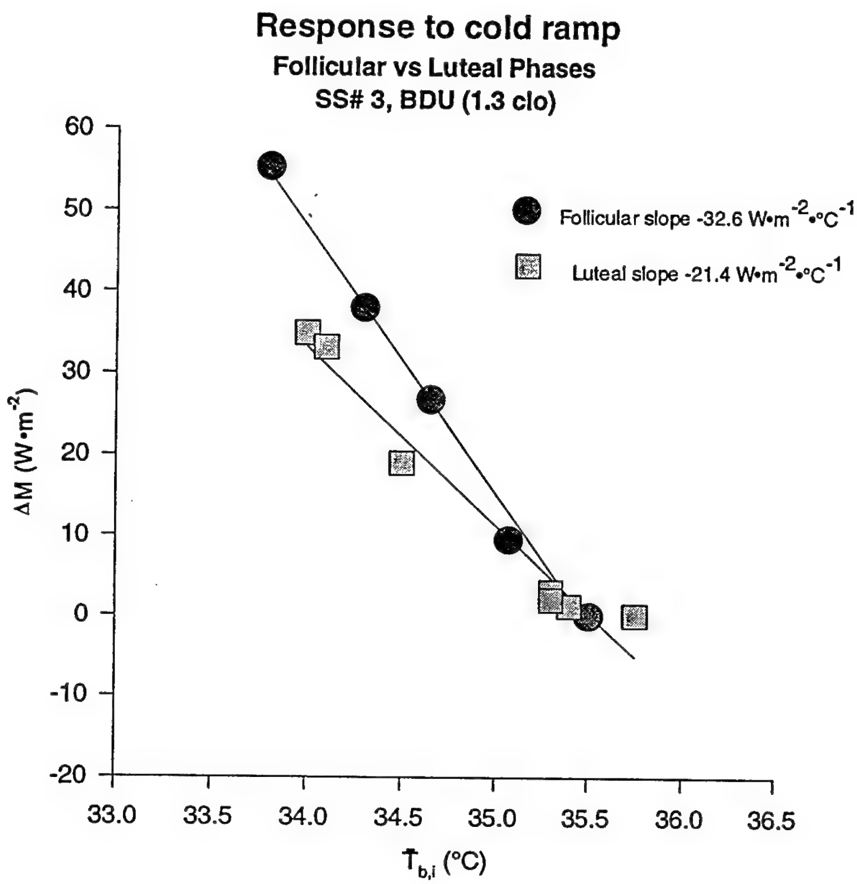


Figure 4. ΔM plotted as a function of integrated mean body temperature ($\bar{T}_{b,i}$) in a representative subject during a cold ramp

Table 2 shows the results from all the subjects when dressed in BDUs. Slope of shivering thermogenesis response to integrated mean body temperature drive during the luteal phase of the menstrual cycle in the women was attenuated ($P<0.02$) but the internal body temperature intercept was unaltered.

Table 2. Comparison of Shivering Responses ($\Delta M = M - M_{basal}$, $W \cdot m^{-2}$) to Integrated Mean Body Temperature thresholds ($\bar{T}bi,o$ °C) during Cold Ramp in 6 women dressed in Battle Dress Uniforms (BDU).

Subj	Slope($W \cdot m^{-2} \cdot K^{-1}$)		Threshold ($\bar{T}b,o$, °C)	
	Follicular	Luteal	$\bar{T}bi,o$ Fol	$\bar{T}bi,o$ Lut
1	-22.52	-12.52	35.38	35.40
2	-40.09	-23.35	35.24	35.48
3	-32.58	-21.39	35.47	35.58
5	-35.50	-27.51	35.68	35.48
6	-38.46	-32.85	35.17	35.49
7	-53.17	-22.12	35.29	35.55
Mean	**-37.05***	**-23.3***	**35.37†**	**35.49†**
±SD	**10.05**	**6.79**	**0.18**	**0.03**

*P < 0.02, Tukey's Test. Significantly different slope between phases;

† Not Significant

Heat Flux

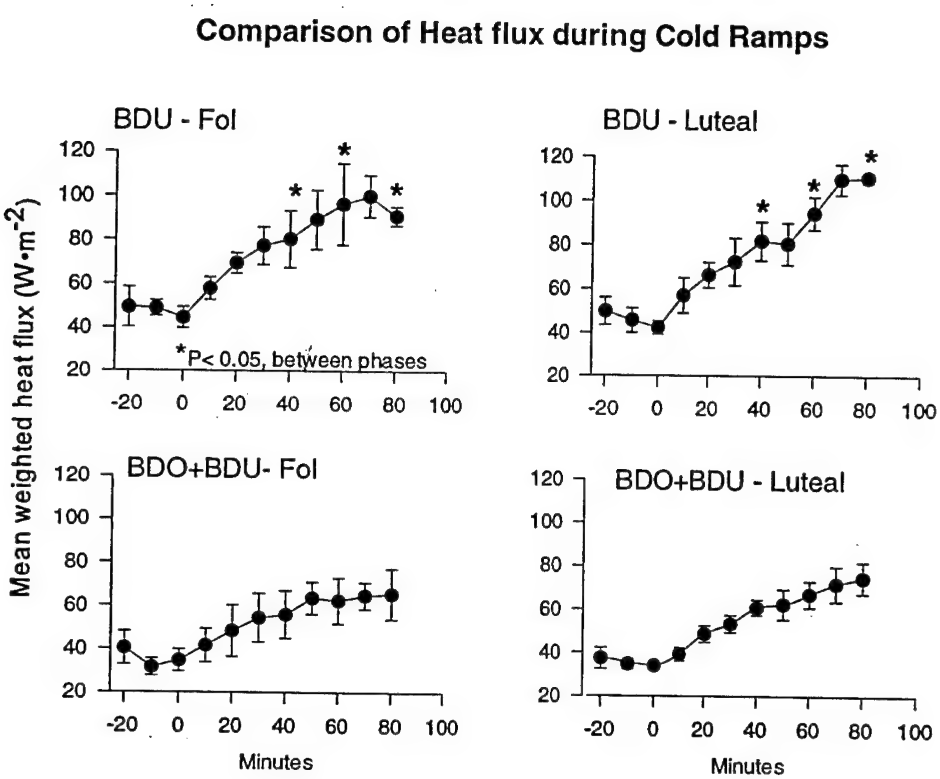


Figure 5. Mean weighted heat flux vs. minutes of cold ramp in all the subjects. Noticeable is the elevated heat flux in the luteal phase experiments apparent when wearing the BDU.

Figure 5 shows the weighted heat flux data from all the runs. During the cold ramp with BDUs in the luteal phases of the women, the threshold for the initiation heat flow through the garment occurred at an equivalent time point (12-13 mins) as in the follicular phase experiments of the women. However, into the 20th minute of the cold ramp ($T_o \approx$ 12°C), heat flux became displaced toward a higher level in the luteal phase than in the

follicular phase (P<0.05) and showed augmented sensible heat flux in the luteal phase with the BDU, remaining so throughout the time periods of 40, 60, and 80 mins of the ramp (P<0.05). Final levels of mean weighted heat flow were higher with the BDUs as compared with the BDO+BDU experiment within each phase (P<0.05).

Rate of Heat Debt

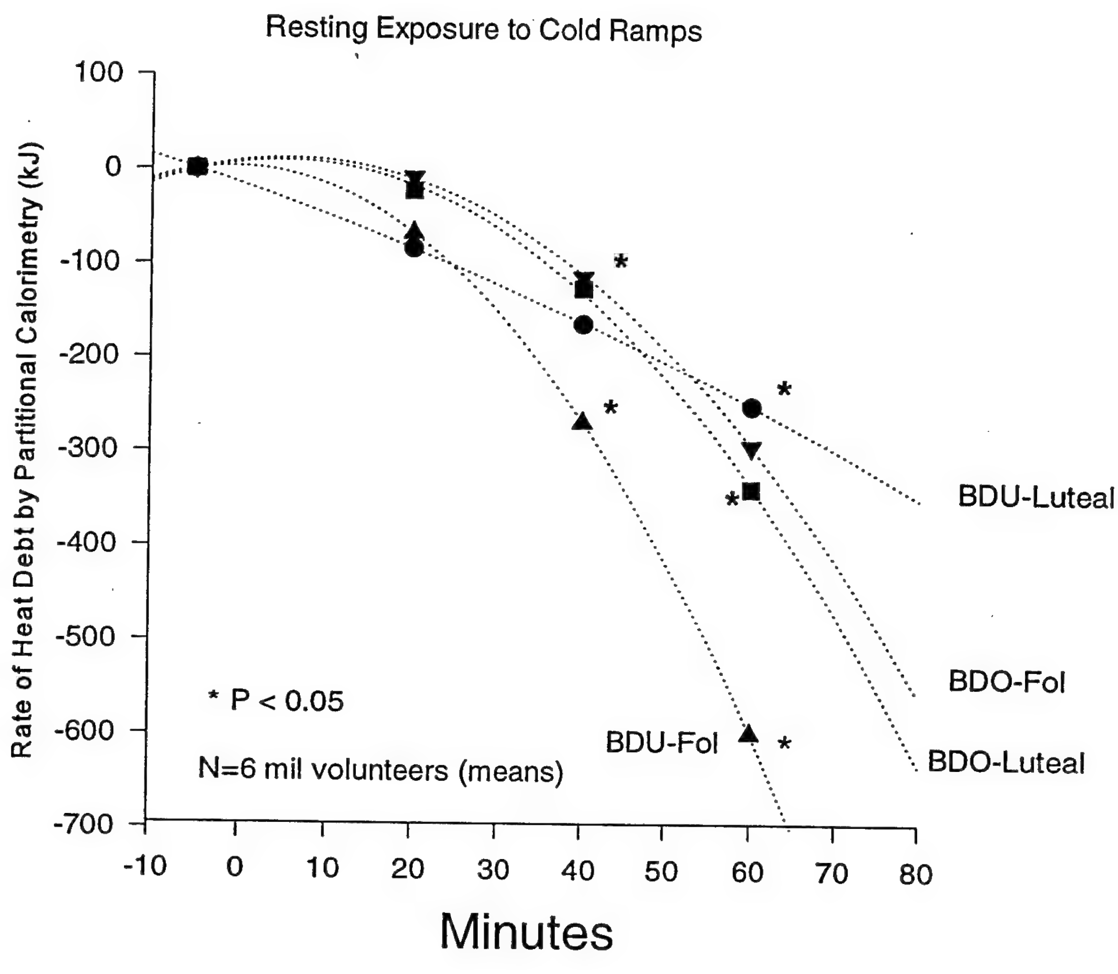


Figure 6. Rate of heat debt determined for all experiments during the cold ramp.

Figure 6 shows that stages of the menstrual cycle and clothing insulation were important modifiers of the whole body rate of heat debt (kilojoules, kJ) determined by partitional calorimetric analyses taking into account each women's M, body weight, %Body Fat and surface area, T_{es}, and $\bar{T}_{sk}$.

Observations of Cold Induced Vasodilation (CIVD)

Figure 7 shows the typical responses found in three of six women "responders,"

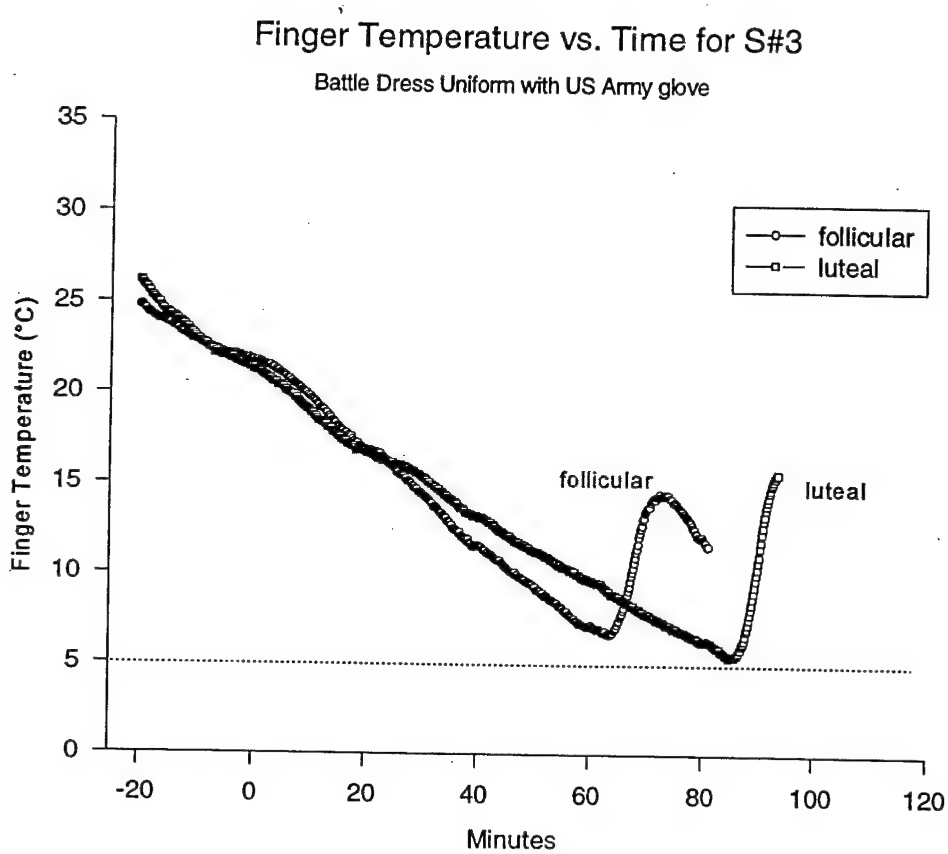


Figure 7. Finger temperature plotted as a function of minutes of cold ramp in a subject demonstrating CIVD during the follicular and luteal phase.

classified as individuals displaying CIVD,(in which the finger nail bed rises by no less than 0.5 °C), following a period of vasoconstrictor activity. In the subject shown, effect of the cold ramp during the follicular phase produced a cooling of the finger down to about 7°C followed by a rapidly increasing vasodilation up to a peak of about 15 -17 °C (Δ8°C within 10min) and another decline. In the luteal phase experiment using this volunteer, the initial finger temperature followed a similar decline as observed in the follicular phase during the first 40 minutes of the ramping, but remained at a higher level than in the follicular phase for the next 50 minutes. There occurred a lag in time of about 20 min, until finger temperature cooled to about 6.0 °C, before the CIVD occurred, which was then followed by the rapid rise in finger skin temperature under the gloved hand. In three other women this equivalent amplitude of the CIVD response was not observed in all experiments nor in all subjects. CIVD was observed in four of the six subjects when dressed in the BDO+BDU (with the similar thermal resistance of the glove) in the follicular phases but not in the luteal phases. Figure 8 shows the variations in CIVD thresholds and the maximal responses observed toward the final minutes of the ramps. Subject 1 showed two separate CIVD cycles during her follicular phase experiment dressed with BDO+BDU garment (albeit her data were not utilized when dressed in BDUs due to thermocouple failure). Limitations placed by Human Use Research Committee regulations to end experimentation at the will of a subject, even before finger temperatures reached 5°C, did not allow us to follow CIVD responses in two women.

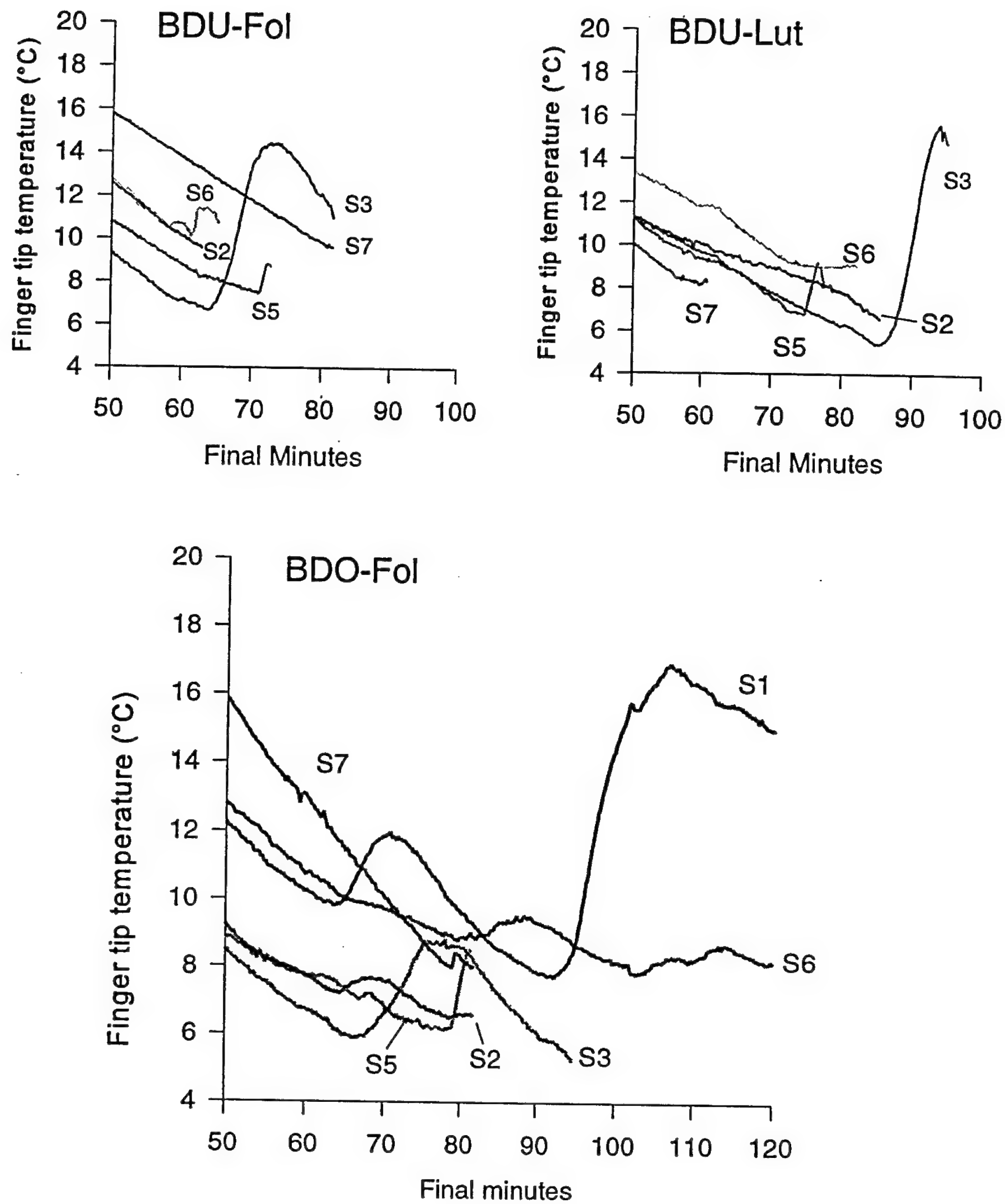


Figure 8. Variations in CIVD response observed during final minutes of the ramp.

Prediction equations for shivering thermogenesis (ΔM, $W \cdot m^{-2}$).

Algorithms quantifying ΔM as a function of the critical skin and core temperature thresholds and control constants were developed from the data set by maximum likelihood parameter estimation (with $r^2 > 0.9$)(Systat, 1992). In the luteal phase, T_{fing} and $\bar{T}_{sk}$ thresholds (21.5°C & 31°C, respectively) affecting excess heat production due to shivering thermogenesis (ΔM) were found to be offset to a lower temperature compared to the follicular phase ($P \leq 0.002$). T_{fing} was shown to be a significant peripheral multiplier of the response. For the experiments in which the women wore the lighter weight clothing (BDU: $I_T = 1.3$ clo; $R_T = 0.2\ m^2 \cdot K \cdot W^{-1}$) at the two distinct stages of their menstrual phase, these equations are:

Follicular Phase (day1-6):

$$\Delta M_{fol} = [0.35 \cdot (\bar{T}_{sk} - 32.5) - 0.85 \cdot (T_{es} - 36.9)] \cdot 0.9 \cdot (T_{fing} - 26.5) \quad , W \cdot m^{-2} \qquad \text{eq (1)}$$

$r^2 = 0.91$, Sum of Squares Residual (SSR)= 1776

Luteal Phase (day 19-25):

$$\Delta M_{lut} = [0.65 \cdot (\bar{T}_{sk} - 31.0) - 2.28 \cdot (T_{es} - 36.9)] \cdot 0.59 \cdot (T_{fing} - 21.5) \quad , W \cdot m^{-2} \qquad \text{eq (2)}$$

$r^2 = 0.86$, SSR=2200

DISCUSSION

Since 1983, specific attention has been directed toward the modeling requirements of individuals working in temperate and warm environments. Little efforts have been focused on ways to characterize physiological mechanisms during cold stress in women and relate these to an acceptable thermoregulatory model formulation. Prediction of shivering thermogenesis by using the various thermoregulatory model equations has not specifically focused on explaining responses owing to the luteal phase offset in internal body temperature (Kolka and Stephenson,1996). Additionally, many of these models to date have not fully incorporated responses due to the separate influences of cold fingers and cold toes (acral drives). During cold weather field operations, the hands and feet are the probable locations of thermal discomfort, local cold injury, and loss of sensation or dexterity which affects performance. As a consequence, the local temperatures of finger and toes are disproportionately important in terms of maintaining thermal comfort, improving morale and performance. Since it is impossible to obtain experimental data for all possible combinations of clothing, handwear and environmental conditions, a model, based on experimental data, for predicting soldier endurance times in the cold has considerable military significance.

CIVD Observations

One current model (Shitzer et al., 1996) predicts the maximum endurance times for an individual based on calculated values for finger temperatures. The model is based on a scenario with and without cold-induced vasodilation (CIVD) response and predicts blood flow to the extremities during the response. Additions needed to the model require

morphological features of finger and hand sizes and autonomic control characteristics expanded to females since we have shown in this study that there is a differential response in cutaneous heat loss during the various stages of the menstrual cycle in females. It could be that augmented hormonal activity (elevated progesterone and/or estradiol) in the luteal phase interacts with local chemical mediators modifying α_2-adrenoceptors. In the luteal phase there could be a blunted delay in the ability of norepinephrine released at specific vascular sites to induce contraction of smooth muscle at cold temperatures (Flavahan; Furchgott, 1993; Hassan and Tooke, 1987; Koenig et al., 1995). The observations in this study suggest further experiments on intact extremity sites or using isolated blood vessels to elucidate mechanisms of response characterizing differential effects of estradiol or progesterone blood levels on arteriovenous-anastamoses (AVAs) receptors during CIVD.

Body Heat Content

As shown in this study, variations in heat content of the thermal system (Vallerand et al., 1992; Gagge and Gonzalez, 1995) (Figure 6) provided as valuable an indicator of cold stress as peripheral vasoconstriction observed in the extremities. The women in our study were similar in body fat (23.9 ±2.4%), so the influence of excess heat flux occurring in the luteal phase by addition of a finite thermal resistance due to clothing was easily partitioned (Figure 5). Our data show that when the influence of body fat is controlled, there may be an imbalance in heat loss compared to heat production mechanisms.

The results using the cold transient technique show that, following a time point in

which heat flux responses are equivalent in women with similar thermal insulation (BDU) and %BF, a definite activation and separation of excess heat loss occurred in the luteal phase (Figure 5). This finding is at variance with steady-state studies of women exposed to 90 min of a 28°C ambient temperature showing decreased thermal conductance in the luteal phase (Frascarolo, et al., 1990). These authors suggest that the offset in core temperature results from an increase in specific thermal insulation. Our data show that such an observation of reliance on thermal insulation per se is probably not in effect when peripheral cold receptor activity dominates in resting women when both thermal insulation and %body fat are sufficiently controlled. The thermal transient analyses favor the hypothesis that increased heat loss is stimulated potentially by the action of estradiol and/or progesterone or cytokines in the luteal phase, possibly altering cellular dynamics of thermosensitive neurons in the hypothalamus. Such observations have been demonstrated in studies with isolated brain slices and have sufficient foundation in many neuronal models (Boulant and Silva, 1989; Cannon and Dinarello, 1985). If cutaneous heat loss reflects a concomitant effect of augmented peripheral blood flow, then the heat flux responses found in the present data (Figure 5) definitely concur with studies showing increased arm blood flow in the luteal phase (Hassan et al., 1987; Hessemer and Bruck, 1985a; Kolka and Stephenson, in press).

It is generally accepted that women in the follicular phase of their menstrual cycle exhibit thermoregulatory functions and physical performance comparable to men when adjusted by body size and maximal aerobic capacity. However, even in the follicular phase

there are other factors in women that may play a part in controlling heat exchange of women in response to cold. Burse (1979) pointed out that morphological differences of women (20% smaller body mass, 14% more body fat, 33% less lean body mass, but only 14-22% less surface area) impinge greatly on their relative ability to balance body heat production and losses. The attenuation of shivering thermogenesis per integrated core temperature ($T_{b,i}$) in the luteal phase in resting women wearing BDUs, accompanied by an excess heat loss response and blunted rate of heat debt, also implies a neuronal influence of estradiol and progesterone blood levels possibly on thermally sensitive neurons in the preoptic/anterior hypothalamus, abating shivering but provoking excess heat loss (Boulant and Silva, 1989).

Whole Body Thermoregulatory Models useful for Cold-Air Stress Responses

Past thermoregulatory models have incorporated shivering algorithms, primarily applicable for unclothed men, determined as a function of core and mean skin temperature response (Stolwijk-Hardy, 1977; Wissler, 1985). Some recent progress has been accomplished toward factoring other variables such as % body fat, lean body mass, and rate of change of skin temperature (Tikuisis and Gonzalez, 1988; Tikuisis et al., 1988; Tikuisis et al., 1991; Hayward et al., 1977; Timbal, 1976). Table 4 shows algorithms examined from some of these cold stress prediction equations that are pertinent to compare with the results from our present study.

Table 4. Algorithms of Various Predictive Models for Cold Stress in the Current Woman Study

†Present algorithms:	Follicular:	$\Delta M\ (W{\bullet}m^{-2}) = [0.35{\bullet}(\bar{T}_{sk} - 32.5) - 0.85{\bullet}(T_{es} - 36.9)]{\bullet}0.9{\bullet}(T_{fing} - 26.5)$
by MLE	Luteal:	$\Delta M\ (W{\bullet}m^{-2}) = [0.65{\bullet}(\bar{T}_{sk} - 31.0) - 2.28{\bullet}(T_{es} - 36.9)]{\bullet}0.59{\bullet}(T_{fing} - 21.5)$
Tikuisis 1991		$\Delta M/lbm = \{0.0422{\bullet}(35.36 - \bar{T}_{sk})^2\}/(\%BF)^{0.506}$
Timbal 1976		$MR\ (W{\bullet}m^{-2}) = 41.31 - 5.01{\bullet}(\bar{T}_{sk} - \bar{T}_{sk,o}) - 57.77{\bullet}d\bar{T}_{sk}/dt$
Hayward 1977		$MR(W{\bullet}kg^{-1}) = 0.0356{\bullet}(\bar{T}_{sk} - 41.8)(T_{es}{}^{*} - 41.0)$
Stolwijk/Hardy1977		$\Delta M\ (W{\bullet}m^{-2}) = [13(T_{es^*} - 37.0) + 0.4(\bar{T}_{sk} - 34.0)]{\bullet}(\bar{T}_{sk} - 34.0)$

$^*T_{es}$ substituted for T_{ty} and T_{cor} of original equation parameters; lbm=lean body mass;%BF= per cent body fat. Data for input to the various models were from separate follicular and luteal phase experiments.†from Maximum Likelihood Parameter Estimation (MLE).

Figure 9 shows the prediction of shivering thermogenesis from the various models applied to the specific body temperatures observed during cold transient of the present study. All prediction models have been normalized to reflect ΔM (in $W{\bullet}m^{-2}$) as previously described (Tikuisis et al.1988).

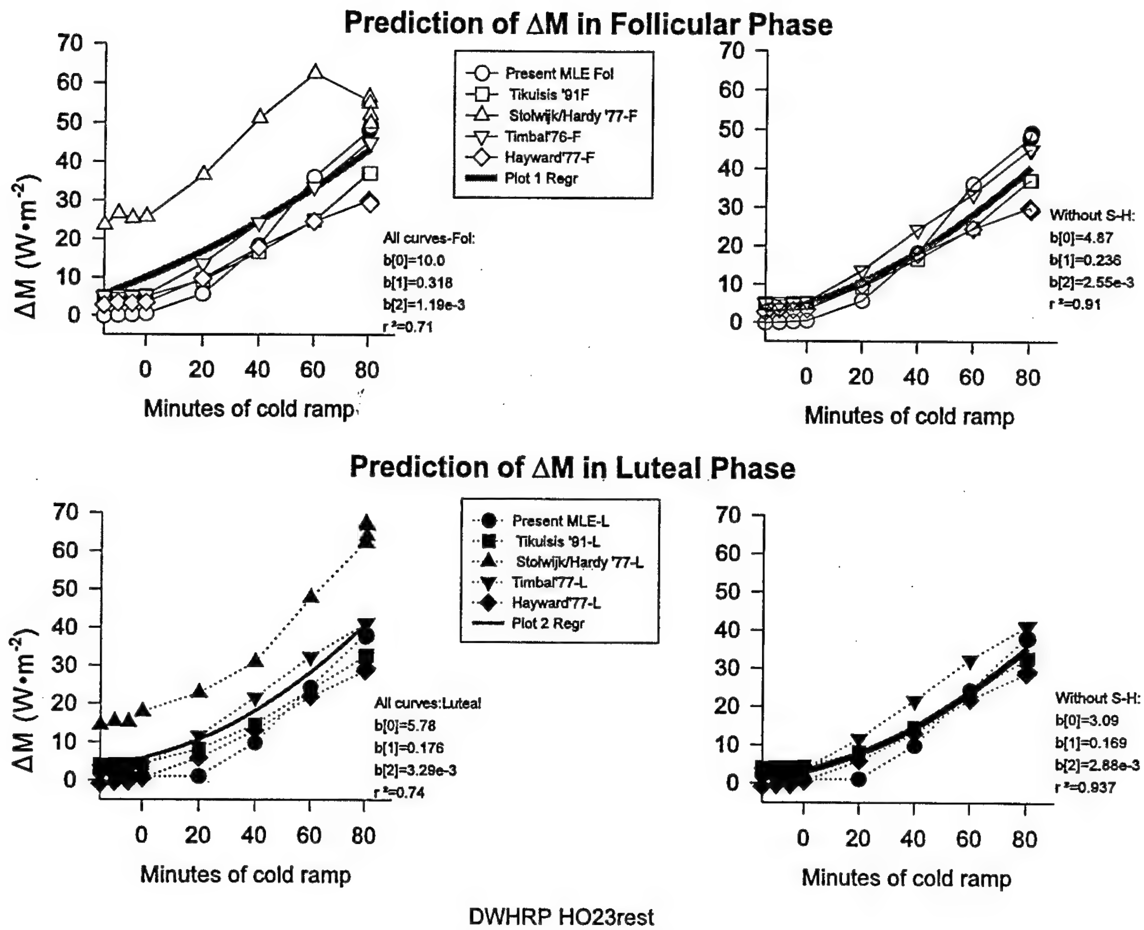


Figure 9. Comparison of four cold stress models to present study data. Right panel shows combined regression analysis without inclusion of Stolwijk-Hardy algorithm .

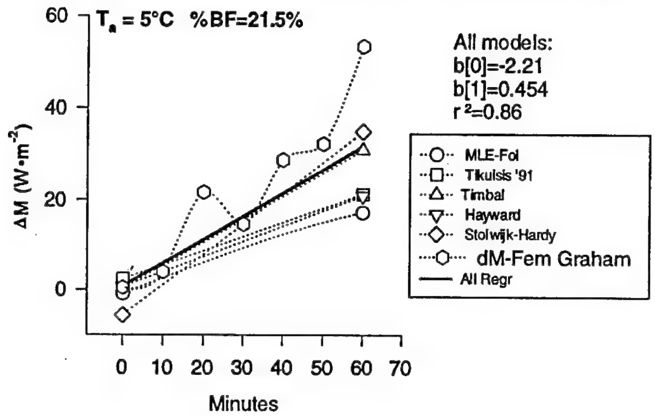
Our data suggest that temperatures from acral sites, independent from a given core site and a mean weighted skin temperature ($\bar{T}_{sk}$), should definitely be considered in any whole body thermoregulatory models describing ΔM effects in resting women (and presumably in men also). This response was adequately simulated by use of parameter estimation analysis confirming that finger temperature is a significant amplifying factor in any cold shivering thermogensis along with %BF (which is the primary attenuator of the response), and lean body mass (Tikuisis, 1991; Timbal, 1977). Early studies by Carlson and others (Carlson, et al., 1971) in men alluded to the effect of local finger temperature having a critical effect on shivering thermogenesis. Studies on various animal species have concurred with this conclusion (Gonzalez et al., 1971; Simon,et al., 1986). The rabbit ear has been shown to be a reliable analogue of skin blood responses occurring in the human hand as well (Gonzalez, et al. 1971).

Figure 9 shows that of the four whole body algorithms predicting shivering thermogenesis as a function of minutes of the present cold ramp, determined exclusively from a cold stress database in unclothed men, the Stolwijk-Hardy equation (1977) proved the most over predictive. However, the models formulated by Tikuisis et al. 1991 (%BF), Timbal (rate of change of skin temperature), and Hayward's (multiplier of core and skin temperatures from a thermal convergence component) were very predictive of the responses observed in women dressed in BDUs during both phases of the menstrual cycle. This preliminary observation suggests that during mild drops in core body temperature either of the latter three cold-air model algorithms may be adequately utilized

as acceptable operational indices (but not mechanistic indicators) of excess shivering response in both males and females.

All the above models and the present study's algorithm were compared to data from an independent study of men and women exposed to steady-state cold stress of 5°C (Graham et al., 1989). Graham studied eumenorrheic, amenorrheic, and men dressed in PT clothing exposed for one hour in the cold during rest and exercise. Figure 10 shows their metabolic heat production data (normalized to ΔM, $W \bullet m^{-2}$) compared with the various cold-air model predictions using results from the eumenorrheic women (%BF= 21.5 %) and men (%BF=8.9%). Rectal temperature was used in place of the various core temperature sites of the various models.

Model Predictions of Cold Stress Data
(Women subjects from Graham et al. J.Appl. Physiol.,1989)



Model Predictions of Cold Stress Data
(Male subjects from Graham et al. J.Appl. Physiol, 1989)

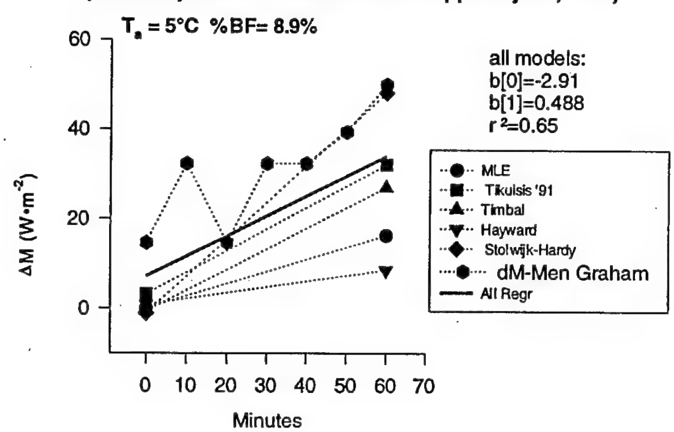


Figure 10. Comparison of model ouput to data from resting men and women of Graham et.al., 1989.

The shivering thermogenesis data observed from the women predicted very adequately up to the first 50 min of steady-state cold stress using the different models (including the Stolwijk-Hardy algorithm) with a combined regression coefficient of determination, r^2=0.86. Observations from the male data in Graham's study were less predictive (r^2 = 0.65) of the data using the various models. The highest predictors of the data were the following: the Stolwijk-Hardy algorithm, the Tikuisis' model which incorporates %BF in its development, Timbal's algorithm, and the present maximum likelihood estimation (MLE) prediction. In the latter MLE equation, toe temperature recorded from the Graham paper was used in lieu of finger temperature in the model. Eumenorrheic women were assumed to be in the follicular phase.

For a combined consolidated thermal model, the Tikuisis (1991) equation appears to be a suitable first approximation strategy that can be used for depicting shivering thermogenesis if peripheral (finger) temperatures cannot be determined as input to model shivering thermogenesis. The algorithm is especially useful in predicting ΔM provided the dominant thermal drive is not from decreasing core temperature and individuals are within a range of %BF between $\geq 8\% \leq 30\%$.

CONCLUSIONS

1.) The decreased slope observed when shivering thermogenesis was plotted as a function of integrated mean body temperature suggests that, (during mid-Luteal and Luteal phases), the elevated internal body temperature and enhanced endogenous estradiol and/or progesterone possibly attenuate the peripheral sensitivity (cold skin thermal drives) to hypothalamic-mediated thermal signals (possible inhibiting either cold sensitive or stimulating warm sensitive neurons) influencing ΔM.

2.) The greater heat flux response and effect on local CIVD response observed in the luteal phases confirms results shown before in women relative to Skin Blood flow (Hessemer and Bruck, 1985b; Kolka and Stephenson, in press). These results suggest CNS-mediated effects on thermosensitive neurons consistent with facilitating heat loss and inhibiting heat production as a function of lowered integrated mean body temperature.

3.) Finally, the pattern of shivering response in resting women at various stages of the menstrual cycle appears optimally modeled by combining fine control (a weighting from local acral peripheral drives, determined by extremity temperatures) in association with core and mean skin temperature. When it is not possible to integrate all key body thermal variables, several cold-air models which incorporate %Body Fat, diverse thermal signals from various core sites, and skin temperature inputs can serve as reliable predictors of shivering response over a limited scope of operational and environmental levels for either men or women.

APPENDIX

Evaluation of integrated mean body temperature is best analyzed from the heat balance equation

$$\Delta \bar{T}_b,i/\Delta t = \frac{[M-(W)-(R+C)-E_{sk}]\bullet A_D}{0.965\bullet m_b} \quad ,°C$$

Where 0.965 W•h/(kg•°C) is the specific heat constant, m_b is body weight, kg, A_D is the DuBois surface area (m^2) and the energy exchange terms in brackets (all in W•m^2) are evaluated by partitional calorimetry.

For every time point dt

$$\Delta \bar{T}_b,i = \frac{[\alpha \bar{T}_{sk} + \beta T_{es}]}{\alpha+\beta} + \sum_0^t(\Delta \bar{T}_b/\Delta t)dt \quad ,°C$$

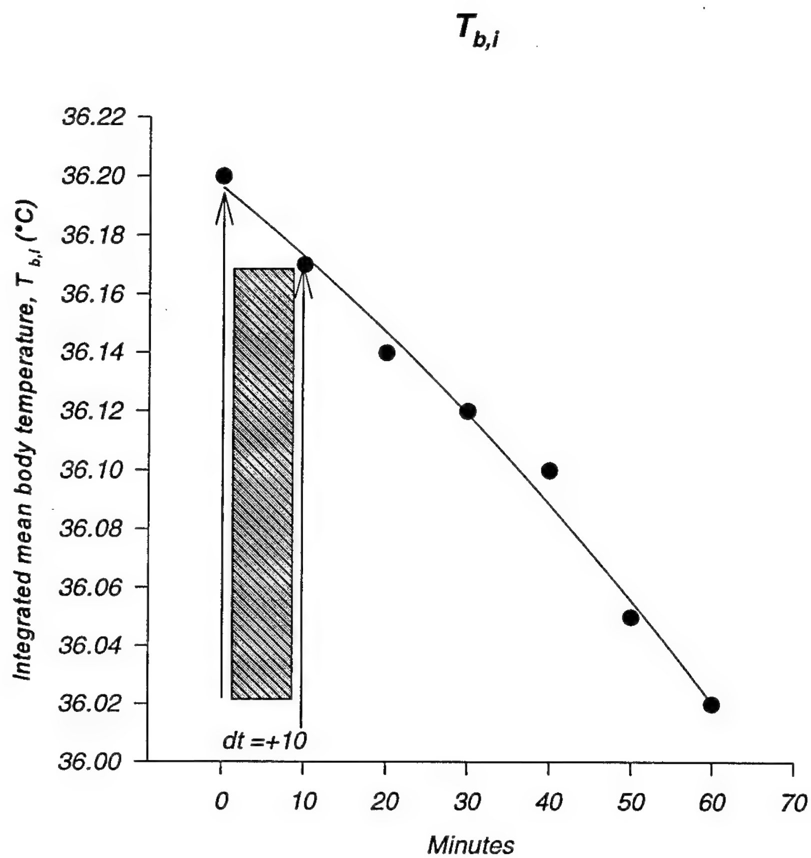
Consider the typical example of a resting woman exposed to a downward ramp in air temperature:

where mean skin temperature ($\bar{T}_{sk}$) is 33°C, esophageal temperature (T_{es}) is 37°C, M - (R+C) - E_{sk} is 47 W•m^{-2}, surface area is 1.54m^2 and body weight is 54 kg.

$\Delta\bar{T}b/\Delta t = (47 \cdot 1.54)/(0.965 \cdot 54) = -1.35$ °C/h or -0.225 °C/min

In 10 min the drop amounts to -0.0225 °C from base temperature at time 0.

The Tb,i at time 10min is thus $(0.2 \cdot \bar{T}sk + 0.8 \cdot Tes) - 0.0225$ or 36.17°C



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